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Original Study

Prevalence and Correlates of Neuropsychiatric Symptoms in Nursing Home Patients With Young-Onset Dementia: The BEYOND Study



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A B S T R A C T

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Objective: Young-onset dementia (YOD) is defined as dementia that develops before the age of 65. Neuropsychiatric symptoms (NPS) have important clinical consequences for patients and their family members. To date, knowledge about the prevalence and correlates of NPS in YOD is limited, but essential to establish specific tailored care for patients with YOD. The aim of this study was to explore the prevalence and correlates of NPS in nursing home residents with YOD.

Design/Setting: Cross-sectional cohort study in Dutch long-term care facilities providing specialized care for YOD.

Participants: Participants included 230 institutionalized patients with YOD.

Measurements: NPS were assessed using the Cohen-Mansfield Agitation Inventory (CMAI) and the Neuropsychiatric Inventory-Nursing Home version (NPI-NH). The influence of gender, dementia severity, type of dementia, and disease awareness on clusters of relevant NPS was investigated using multivariate logistic regression analysis and subsequently corrected for the possible confounders of age, duration of institutionalization, and psychoactive medication use.

Results: Ninety percent of the nursing home residents with YOD showed 1 or more neuropsychiatric symptoms, 88% showed significant agitation, and 56% showed relevant apathy. No gender differences were found. Although physically aggressive behavior, non-physically aggressive behavior, and apathy were more common in patients with (very) severe cognitive decline (Global Deterioration Scale [GDS] stage 6–7), verbally agitated behavior was common in patients in all except the most severe stages of dementia (GDS 2–6). Apathy was more prevalent in alcohol-related dementia. Low levels of awareness were associated with more physically aggressive behavior and aberrant motor behavior.

Conclusion: The prevalence of NPS was high and was associated with the severity and type of dementia and disease awareness. Agitation and apathy are the most important symptoms to focus on in YOD. The high prevalence of NPS supports the idea of care delivery in special care units. Further research is needed on potentially influencing environmental correlates of NPS in YOD.

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Young-onset dementia (YOD), dementia developing before the age of 65, is recognized as an important clinical and social problem, with serious consequences for both patients and their caregivers. The

presence and type of neuropsychiatric symptoms (NPSs), such as agitation, apathy, and depression, have a severe impact on patients and their families. NPSs are the most important risk factor for

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caregiver burden and institutionalization.^{1,2} Understanding the prevalence and determinants of NPSs in institutionalized patients with YOD is important for treatment and planning of services, so as to improve quality of life of institutionalized patients with YOD and their (professional) caregivers.

The clinical manifestation of YOD differs from that of late-onset dementia (LOD) due to a wider range of etiologies and the younger age itself.³ Although Alzheimer disease (AD) is the most common cause, there is a higher prevalence of frontotemporal dementia (FTD), alcohol-related dementia, and Huntington disease in patients with YOD.^{3–5} These etiologies may differ in clinical presentation, course, and prevalence of specific NPSs.⁴ Some studies have suggested that YOD may display a higher prevalence of NPSs than LOD, possibly related to the more unexpected loss of independence and active social roles at younger age.^{6,7} Yet, there are only a very few studies that directly compare prevalence rates of NPS in YOD with LOD, with inconsistent results so far.^{8–10} These studies only included patients with AD, mainly in the early stages. Two studies found fewer and less severe NPSs in YO-AD than in LO-AD,^{8,9} whereas the third study comparing YO-AD with LO-AD found more NPSs in younger patients with AD.¹⁰ Because of the heterogeneity of these studies, these inconsistencies are difficult to interpret.

Only a few studies have investigated which factors are correlated with NPS, most of which are performed among patients with LOD. Increased severity of dementia is associated with NPS in nursing home residents with LOD. Symptoms, such as agitation, aggression, and apathy, were more frequently present in patients showing (moderately) severe cognitive decline.^{11–13} Gender was also a determinant of agitation in nursing home residents with LOD: physically aggressive behavior was more common in men,¹⁴ whereas female patients showed more verbally agitated behavior.¹¹ Because the institutionalized YOD population consists of more men than in LOD, this might be related to NPS prevalence in YOD. As mentioned before, the more variable types of dementia in YOD may also be associated with the prevalence of NPS.^{3,4} For example, the relatively high prevalence of FTD may cause a higher prevalence of NPSs, such as disinhibition, eating behaviors, and stereotyped behaviors.¹⁵ Another related factor influencing NPS in YOD may be disease awareness. It is suggested that patients with YOD have more awareness of their condition than patients with LOD.¹⁶ Awareness of cognitive, functional, and social deficits might evoke emotional reactions and NPSs. The study found that high awareness in community-dwelling patients with YOD was associated with a higher risk of depressive symptoms.¹⁶ The prevalence of NPSs also may be associated with the use of psychoactive medication. In community-dwelling patients with YOD, psychoactive drug use is relatively high.¹⁷ There is no literature of the prevalence of psychotropic drug use and the relationship with NPSs in YOD in institutionalized patients. Studies of patients with LOD show a high prevalence of psychotropic drug use in institutionalized patients with dementia.^{12,18,19}

This study aimed to assess the prevalence and correlates of relevant NPSs in institutionalized patients with YOD. We hypothesized that there may be an association with gender, dementia severity, dementia subtype, and disease awareness.

Methods

Study Population

This study is part of the Behaviour and Evolution in Young Onset Dementia (BEYOnD) study. The BEYOnD study is a cross-sectional cohort study into the functional characteristics and correlates among 230 patients with YOD admitted to long-term care facilities. Patients were recruited between 2005 and 2009 from 8 Dutch nursing homes (from different regions in the country, urban as well as rural

areas) delivering specialized YOD care and participating in the Dutch National Steering Committee for Younger People with Dementia.

Patients were considered for inclusion if (1) they met criteria for dementia according to the DSM-IV-TR,²⁰ (2) the first documented symptoms were present before the age of 65, and (3) they were residing in the nursing home for at least 4 weeks. At inclusion it was allowed that patients were older than 65. If patients met all criteria, informed consent was obtained from the patient or his or her legal guardian/representative.

The study protocol is in accordance with the declaration of Helsinki, with the Dutch legislation on medical research and it is in agreement with the Conduct Health Research of the Dutch federation of Biomedical Scientific Societies. The study protocol was approved by the Regional Medical Ethics Review Committee Arnhem-Nijmegen. The committee stated that, in accordance with Dutch legislation, the study could be performed without a review procedure by the committee because in the study, only observational data gathered by nursing staff as part of their daily work were used.

Data Collection

Baseline characteristics were retrieved from patients' medical records.

On the day of inclusion, vocational nurses specifically assigned to individual patients were interviewed by the researcher (AM, elderly care physician)²¹ and a research assistant (psychologist).

Assessment of Dementia Subtype

The diagnosis and dementia subtype were retrieved from the medical record. The type of dementia was recorded as stated in the medical record, in the original diagnostic letter from the physician who established the diagnosis, according to the applicable criteria. Most patients had an adequate medical work-up determining the type of dementia, including neurological and neuropsychological tests and imaging at a memory clinic. If this was not the case, then diagnosis was recorded as not otherwise specified.

The types of dementia were categorized into AD, vascular dementia (VaD), FTD, alcohol-related dementia (AlcD), and "other causes" of dementia, including Lewy body disease, Huntington disease, dementia caused by acquired brain injury, and encephalopathy.

Assessment of Dementia Severity

The severity of the dementia was assessed by the Global Deterioration Scale (GDS), consisting of a 7-point scale (1–7) ranging from "no cognitive impairment" (1) to "very severe cognitive impairment" (7). GDS scores of 4, 5, and 6 denote moderate, moderately severe, and severe cognitive decline. This scale is widely used for the assessment of dementia severity and correlates well with behavioral, neuro-anatomic, and neuropsychological measures.²²

Assessment of Disease Awareness

Awareness was assessed with the Guidelines for the Rating of Awareness Deficits (GRAD) defining impaired awareness as the absence of explicit knowledge or recognition of one's own cognitive deficits.²³ The GRAD is a reliable and valid semistructured assessment of the degree of awareness by comparing the patient's and the caregiver's histories on patient's functioning and complaints. Awareness was rated on a 4-point scale: 4 (intact), 3 (mildly disturbed), 2 (moderately disturbed), and 1 (severely disturbed). Patients without any meaningful communication were rated as 0. For the logistic regression analysis, awareness was dichotomized in any awareness

(intact, mildly disturbed, or moderately disturbed) versus severely disturbed awareness or no communication.

Assessment of Psychotropic Drug Use

Data on the use of psychotropic drugs on the day of assessment were registered. Psychotropic drug use (PDU) was classified using the Anatomical Therapeutic Chemical-classification (Nordic Council on Medicines, 1990)²⁴ and grouped into antipsychotics, anxiolytics, hypnotics/sedatives, antidepressants, and antiepileptics.

Assessment of NPS

The 1-month prevalence of NPS was assessed by 2 caregiver interview instruments with questions regarding NPS in the 4 weeks before the inclusion date.

The presence and severity of NPSs were assessed by the Dutch version of the Neuropsychiatric Inventory–Nursing Home version (NPI-NH),^{25,26} including 12 NPSs: delusions, hallucinations, agitation/aggression, depression, anxiety, euphoria/elation, apathy/indifference, disinhibition, irritability/lability, aberrant motor behavior, nighttime behavior disturbances, and appetite/eating disturbances. After a screening question, both the frequency (F) and severity (S) of each symptom are rated on a 4- (1–4) and 3-point (1–3) Likert scale, respectively. A symptom score is calculated for each symptom by multiplying the frequency and severity scores ($F \times S$ -score), resulting in values ranging from 0 to 12 for each symptom. In accordance with previous studies,^{11,27} NPSs with an $F \times S$ score ≥ 4 are considered clinically relevant. Based on previous studies,^{28–30} we defined neuropsychiatric subsyndromes of agitation and psychosis, by clustering NPI-NH items in a psychosis-cluster (hallucinations and/or delusions) and agitation-cluster (agitation, disinhibition, irritability, and/or aberrant motor behavior).

Agitated and aggressive behavior was further assessed using the Cohen Mansfield Agitation Inventory (CMAI), Dutch version.³¹ This instrument assesses the frequency of 29 agitated or aggressive behaviors and is validated for use in nursing home patients.^{32,33} The frequency of each symptom is rated on a 7-point scale (1–7) ranging from “never” to “several times an hour.” Clinically relevant agitation was defined as behavior occurring at least once a week or more (frequency score ≥ 3). Total CMAI score was obtained from the sum of all item-scores (29–203). CMAI items were clustered into physically nonaggressive behavior, physically aggressive behavior, and verbally agitated behavior, according to the 3-factor solution from a factor analytic study in patients with dementia in Dutch nursing homes,³⁴ corroborating earlier findings on the factor structure of the CMAI.^{32,33}

Analysis

Statistical analyses were performed using SPSS 20 (IBM SPSS Statistics, IBM Corporation, Chicago, IL).

By generating descriptive statistics, the prevalence of NPSs was analyzed in subgroups according to gender, severity of cognitive decline (GDS stages 4–7), dementia subtype, and disease awareness; 95% confidence intervals (CIs) of prevalence were calculated using the Wilson score interval. Univariate analyses were performed (using crosstabs with χ^2 test for categorical variables and with t tests for continuous variables) to screen for associations. A P value less than 0.05 was considered to be statistically significant. Statistically significant variables from the univariate analysis were subsequently analyzed in a multivariate logistic regression analysis, with presence or absence of agitated behavior (frequency score ≥ 3) on the CMAI clusters and the presence or absence of individual and clustered symptoms on the NPI-NH ($F \times S$ cutoff score ≥ 4) as dependent variables. Independent variables entered stepwise were gender, dementia

severity, dementia subtype, and disease awareness, and as correction factors the possible confounders of age, duration of institutionalization, and PDU were added. We obtained multivariate models with at least 1 explanatory variable per 7 events, as suggested by the study of Vittinghoff et al.³⁵ Only independent variables with a sufficient amount of events were added to the logistic regression analysis. To reduce the chance of type I errors, significance was defined as $P < .02$.

Interaction terms (gender \times independent variables) were also entered in the model to allow for possible effect modification, but were left out of the final analysis because they did not reach statistical significance ($P < .02$).

Results

Patient Characteristics

The study population consisted of 230 patients, of whom 5 patients were excluded because of incomplete NPI or CMAI data. Of the remaining 225 patients, with a mean age of 60.1 years, the female-male ratio was approximately 1:1 and the median length of stay in the nursing home was 34 months (Table 1). Most of the patients had severe dementia (GDS 6). AD was the most frequent dementia subtype (31.9%). Two-thirds (66.6%) of the patients had severely impaired or undetectable disease awareness. Psychotropic drugs had been prescribed to 87.6% of the patients, mostly antipsychotics and antidepressants.

Prevalence of NPSs

The prevalence of NPSs is represented in Table 2. Almost all patients showed at least one clinically relevant neuropsychiatric symptom, as measured by the NPI-NH. Three-quarters showed 2 or more NPSs. Most patients had significant symptoms in the agitation cluster of the NPI-NH (66%). Apathy was found in more than half of the patients and depression in one-fifth. Psychotic symptoms were found in 11% of the patients with YOD. Further analysis of agitated behavior with the CMAI clusters showed a prevalence of relevant physically nonaggressive behavior as well as physically aggressive behavior in

Table 1
Patient Characteristics of 225 Nursing Home Patients With YOD

Age: mean	60.1 (SD 7.3) range 39.1–77.8
Gender male: n (percentage)	120 (53.3)
Length of stay in months: mean	33.7 range 1–184
Time between first symptoms and diagnosis in months: mean	46.1 range 0–275
GDS: n (percentage)	
GDS stage 2–4, moderate cognitive decline	39 (17.3)
GDS stage 5, moderately severe cognitive decline	55 (24.4)
GDS stage 6, severe cognitive decline	68 (30.2)
GDS stage 7, very severe cognitive decline	63 (28.0)
Dementia subtype: n (percentage)	
AD	72 (32.0)
VaD	29 (12.9)
FTD and related dementias	36 (16.0)
AlcD	40 (17.8)
Other causes of dementia	48 (21.3)
Awareness, n = 222: n (percentage)	
Absent, score 0–1	148 (66.7)
Any awareness, score >1	74 (33.3)
Psychoactive medication use: total n (percentage)	197 (87.6)
Antipsychotic drugs	112 (49.8)
Antidepressant drugs	111 (49.3)
Anxiolytic drugs	70 (31.1)
Hypnotics/sedatives	40 (17.8)
Antiepileptic drugs	58 (25.8)

Table 2
Prevalence of Neuropsychiatric Symptoms in Nursing Home Patients With YOD

	n (%), CI
NPI-NH significant symptoms ^a	
Delusions	16 (7.1%, CI 4.4%–11.2%)
Hallucinations	13 (5.8%, CI 3.4%–9.6%)
Agitation/aggression	86 (38.2%, CI 32.1%–44.7%)
Depression/dysphoria	44 (19.6%, CI 14.9%–25.2%)
Anxiety	36 (16.0%, CI 11.8%–21.4%)
Euphoria	23 (10.2%, CI 6.9%–14.9%)
Apathy	125 (55.6%, CI 49.0%–61.9%)
Disinhibition	51 (22.7%, CI 17.7%–18.6%)
Irritability	84 (37.3%, CI 31.3%–43.8%)
Aberrant motor behavior	75 (33.3%, CI 27.5%–39.7%)
Nighttime disturbances	26 (11.6%, CI 8.0%–16.4%)
Appetite/eating change	47 (20.9%, CI 16.1%–26.7%)
NPI-NH any significant symptom ^a	202 (89.8%, CI 85.1%–93.1%)
2 or more significant symptoms	167 (74.2%, CI 68.1%–79.5%)
NPI-NH agitation cluster [†]	149 (66.2%, CI 59.8%–72.1%)
NPI-NH psychosis cluster [‡]	25 (11.1%, CI 7.6%–15.9%)
CMAI cluster significant symptoms [§] :	
Physically nonaggressive	136 (60.4%, CI 53.9%–66.6%)
Physically aggressive [¶]	148 (65.8%, CI 59.4%–71.7%)
Verbally agitated behavior ^{**}	115 (51.1%, CI 44.6%–57.6%)
Any significant symptom	197 (87.6%, CI 82.6%–91.2%)

Prevalence of NPS in number and % of 225 patients.

^aAny item with frequency (F) × Severity (S) score ≥4.

[†]One or more significant symptom(s) of agitation/aggression, disinhibition, irritability, and/or aberrant motor behavior.

[‡]One or both significant symptoms of delusions and hallucinations.

[§]Any item occurring once a week or more.

^{||}One or more significant symptoms of pacing, hiding, hoarding, trying to get to a different place, handling things inappropriately, general restlessness, or inappropriate dressing/disrobing.

[¶]One or more significant symptoms of hitting, pushing, scratching, cursing, grabbing, screaming, spitting, and strange noises.

^{**}One or more significant symptoms of constant unwarranted request for attention or help, complaining, repetitive sentences or questions, and negativism.

approximately two-thirds of the patients and verbally agitated behavior in 51% of patients.

Factors Associated With the Prevalence of NPSs

Logistic regression analysis (Table 3) did not reveal significant associations of gender with any NPS (CMAI and NPI-NH items or clusters).

Table 3
Results (OR) of Multivariate Logistic Regression Analysis of the Influence of Gender, Dementia Severity, Dementia Subtype, and Disease Awareness on Agitation and Other Neuropsychiatric Symptoms in Nursing Home Patients With YOD

OR (SD)	Gender, Male = Reference	GDS, GDS Stage 7 = Reference			Disease Etiology, AD = Reference				Awareness, Severely Disturbed = Reference	
		Female	GDS 2–4, n = 39	GDS 5, n = 54	GDS 6, n = 66	VaD, n = 29	FTD, n = 36	Alc, n = 38		Other, n = 47
CMAI ^a										
Physically nonaggressive	1.2 (0.6–2.2)	1.4 (0.4–4.7)	1.1 (0.4–2.9)	3.9 (1.5–10.1)	0.3 (0.1–0.9)	1.8 (0.6–5.4)	1.0 (0.4–2.8)	0.5 (0.2–1.2)	0.5 (0.2–1.1)	
Physically aggressive	0.6 (0.3–1.2)	0.2 (0.1–0.7)	0.2 (0.1–0.6)	0.6 (0.2–1.5)	1.6 (0.4–3.1)	1.1 (0.4–3.1)	1.3 (0.4–3.7)	0.7 (0.3–1.9)	0.4 (0.2–0.9)	
Verbally agitated	1.5 (0.8–2.7)	5.0 (1.6–15.5)	3.0 (1.1–7.9)	3.1 (1.4–6.9)	2.0 (0.7–5.6)	1.2 (0.5–3.1)	1.9 (0.7–5.3)	1.6 (0.6–3.9)	1.0 (0.5–2.0)	
NPI-NH agitation [†]										
Aggression/agitation	1.0 (0.6–1.8)	1.7 (0.5–5.4)	1.2 (0.5–3.2)	1.8 (0.8–3.9)	0.7 (0.3–2.1)	1.5 (0.6–3.5)	0.8 (0.3–2.1)	1.7 (0.7–4.1)	0.5 (0.3–1.1)	
Irritability	0.8 (0.4–1.5)	1.6 (0.5–5.2)	1.6 (0.6–4.4)	2.6 (1.2–6.0)	0.6 (0.2–1.7)	0.5 (0.2–1.4)	0.8 (0.3–2.2)	1.6 (0.7–4.1)	0.7 (0.3–1.4)	
Aberrant motor behavior	1.3 (0.7–2.6)	0.9 (0.2–4.1)	1.2 (0.4–3.8)	2.5 (1.1–5.9)	0.3 (0.1–1.1)	2.4 (0.9–6.3)	0.3 (0.1–0.9)	0.2 (0.1–0.8)	0.2 (0.1–0.6)	
Total	1.0 (0.6–1.9)	0.9 (0.3–2.8)	1.1 (0.4–3.1)	1.6 (0.7–3.9)	0.8 (0.3–2.2)	2.2 (0.7–6.3)	0.7 (0.3–1.9)	0.9 (0.4–2.3)	0.5 (0.2–1.1)	
NPI-NH Apathy [‡]	0.6 (0.3–1.2)	0.1 (0.0–0.3)	0.2 (0.1–0.5)	0.4 (0.2–1.1)	1.2 (0.4–3.4)	1.6 (0.6–4.1)	4.6 (1.5–14.0)	1.1 (0.4–2.9)	0.9 (0.4–2.0)	

After correction for psychoactive medication use, duration of institutionalization, and age. Interaction terms were allowed, but did not appear to be significant ($P > .05$) and therefore were left out of the final analysis.

Bold indicates significant result with $P < .05$ ($R = 1$ not included in logistic regression analysis) in χ^2 test, $df = 3$.

^aAny item occurring once a week or more.

[†]NPI-NH frequency (F) × Severity (S) score ≥4.

NPSs did show associations with dementia severity. Patients with GDS 2 to 4 and 5 were less likely to show apathy compared with patients with GDS 7 with an odds ratio (OR) of 0.1 (CI 0.0–0.3) and 0.2 (CI 0.1–0.5) respectively. For GDS 6, the difference was not significant. Agitation, in all 3 clusters of the CMAI, was associated with dementia severity. In patients with GDS 6, physically nonaggressive behavior was more prevalent compared with GDS 7 (OR 3.9, CI 1.5–10.1), in patients with GDS 2 to 4 and 5 physically aggressive behavior was less prevalent with an OR of 0.2 (CI 0.1–0.7) than in patients with GDS 7, and patients with GDS 2 to 4, 5, and 6 all demonstrated more verbally agitated behavior (OR 5.0, CI 1.6–15.5; OR 3.0, CI 1.1–7.9; and OR 3.1, CI 1.4–6.9, respectively) compared with GDS 7. So, verbally agitated behavior was more prevalent in less severe stages of dementia, whereas physically aggressive as well as nonaggressive agitation tended to be more prevalent in more severe stages of dementia.

NPSs also showed to be associated with the dementia subtype. Patients with AlcD had a higher chance of demonstrating apathy compared with AD (OR 4.6, CI 1.5–14.0). Aberrant motor behavior was less common in AlcD (OR 0.3, CI 0.1–0.9) and other causes of dementia (OR 0.2, CI 0.1–0.8) compared with Alzheimer-type dementia. Patients with YOD with VaD had a smaller chance of demonstrating physically nonaggressive agitation (OR 0.3, CI 0.1–0.9) compared with the other dementia subtypes, whereas physically aggressive agitation showed no association with dementia subtype.

Disease awareness was also associated with NPSs. The presence of intact or mild to moderately disturbed awareness was associated with less physically aggressive behavior (OR 0.4, CI 0.2–0.9) and aberrant motor behavior (OR 0.2, CI 0.1–0.6).

Discussion

This study is the first to describe the prevalence and determinants of NPS in patients with YOD in nursing homes. We found high prevalence-rates of NPS and statistically significant associations with severity of the dementia, dementia aetiology and disease awareness.

Compared to studies with community-dwelling patients with YO-AD, we found a higher prevalence of agitation and apathy.^{8,9} This may be explained by more severe dementia in the nursing home population, by the fact that NPSs are a risk factor for nursing home placement in YOD,² and possibly by the presence of patients with other dementia subtypes, of which other studies have shown that these come with more NPSs than Alzheimer-type of dementia.¹⁵ Nursing home patients

with YOD also demonstrated a higher prevalence on all items of the NPI-NH agitation cluster and of apathy compared with institutionalized patients with LOD.¹¹ Psychotic symptoms were less prevalent in patients with YOD. Two studies directly comparing YO-AD with LO-AD found a lower prevalence of the NPI-NH agitation cluster in YOD.^{8,9} Again, this discrepancy can be explained by the fact that these studies included only community-dwelling patients with YOD with earlier stages of AD. This finding may indicate that the prevalence of agitation and apathy in YO-AD shows a larger increase over the course of the illness than in LO-AD, resulting in relatively more NPSs in institutionalized YOD. It also may be related to the possibility that patients with YOD are admitted in more advanced stages of the dementia. On the other hand, the population in specialized nursing units for YOD may show a selection bias toward patients with YOD with more challenging behavior, for these patients are more likely to be referred to special YOD units because they do not fit in conventional dementia care units.

Apathy was one of the most common NPSs in nursing home patients with YOD, which is consistent with previous findings in both YOD and LOD.^{8,9} and the fact that apathy is a significant predictor of institutionalization.²

Multivariate analysis for correlations with NPS showed no significant gender differences for NPS. This is in contrast with most studies in LOD, reporting more physically aggressive agitated behavior in men.^{11,14} This may be related to our study being underpowered to detect smaller differences. Dementia severity was significantly correlated with NPSs. Physically aggressive or nonaggressive agitation as well as apathy showed the highest prevalence in patients in later stages of dementia. Yet, verbally agitated behavior appeared to be more common in patients in earlier stages of dementia. The finding of a prevalence peak of physically aggressive and nonaggressive behavior in patients with severe cognitive deterioration was also found in a study on patients with LOD in nursing homes¹¹ in which the CMAI clusters physically aggressive, physically nonaggressive, and verbally agitated behavior also were associated differently with dementia severity. This again supports the notion that agitation is not a unitary concept, but can be distinguished into 3 clinically relevant entities, possibly with different therapeutic strategies in LOD as well as in YOD.

Dementia severity also was significantly correlated with apathy as was already demonstrated earlier,³⁶ indicating a positive relationship between apathy and cognitive impairment, functional disability, and overall dementia severity in this YOD population. Several studies with patients with LOD also demonstrated that apathy was correlated with disease severity and functional deficits.^{11,37} The finding that depressive symptoms were not associated with dementia severity supports the notion that depression and apathy are 2 distinct syndromes in both YOD³⁶ and LOD.³⁷

Apathy was correlated with dementia subtype, with a significantly higher prevalence in patients with AlCD. This matches the clinical manifestations of executive dysfunction in Korsakov syndrome. Also, several studies investigating the pathophysiological aspects of AlCD show prominent white matter loss in the prefrontal cortex,³⁸ which may play an important role in apathy.³⁹ We did not find other significant differences in NPSs between AD and other dementia subtypes in the multivariate analysis. This contrasts with earlier findings that non-AD types come with more behavioral problems.¹⁵ Our negative finding may be caused by the relatively small subgroup size.

We hypothesized that NPS would be more prevalent with more disease awareness, but this was not confirmed in our study. Instead, symptoms of physically aggressive behavior and aberrant motor behavior were high in patients with severely disturbed awareness. This association of severely disturbed awareness with increased agitation was seen earlier in patients with LOD,⁴⁰ but never described in patients with YOD. Maybe awareness plays a role in enabling

persons to appraise environmental cues and conform their behavior to social norms. With decreasing awareness they may be unable to adjust their behavior to environmental demands, leading to behavioral symptoms like physically aggressive behavior. These NPSs may also simply represent a consequence of the disease progression, or expression of resistance to care, which may be more prominent in patients with advanced disease.

In contrast to findings in community-dwelling patients with YOD,¹⁶ we did not find an association between high levels of awareness and depressive symptoms. Our population consisted of younger persons with more advanced stages of dementia, and relatively low prevalence of intact awareness (1.8%) or mildly disturbed awareness (10.8%). Therefore, our study was not powered to verify this relationship.

Strengths and Limitations

One of the major strengths of our study is the large and representative sample of nursing home patients with YOD. We performed a structured and extensive assessment of NPSs by using the NPI-NH as well as 3 symptom-clusters of the CMAI for the assessment of agitation.

There are limitations that have to be considered. The population of the special care units for patients with YOD results in possible bias, with overrepresentation of younger persons, showing more behavioral symptoms and/or less severe dementia. People approaching the age of 65, with mild NPSs or with very severe dementia and total dependency may be more likely to be placed in regular nursing homes.

The type of dementia was established before 2009. These diagnoses may therefore not be according to more recent diagnostic standards. This may have influenced the measured prevalence of some subtypes of dementia, such as dementia with Lewy bodies or dementia not otherwise specified. Because inclusion in the study ended in 2009, this may also have affected the high rate of PDU, especially antipsychotics. It might be expected that, based on recent guidelines, PDU has decreased. Preliminary data from several Dutch studies (in preparation) however, showed only a limited decrease of use of antipsychotic drugs in Dutch nursing home patients with dementia. We assume that the changes in PDU will not have affected the primary correlations with NPSs.

Furthermore, the tests used were not specifically validated for patients with YOD. The GDS was originally designed to establish dementia severity in elderly patients with AD. Therefore, it might be less valid for the assessment of dementia severity in younger patients and other dementia subtypes. The GDS is only a global measure to assess the severity of dementia. Assessment of cognition with validated tests may have given a better representation of cognition and dementia severity. Also, the NPI-NH and CMAI are not specifically validated for patients with YOD. Certain behaviors (eg, resistance to care) when observed in a middle-aged man may be interpreted as aggression, whereas this would not be the case if an elderly woman would show the same behavior. The use of the awareness instrument also had the limitation of a large number of patients in whom we could not assess any awareness, because of the absence of any meaningful communication. These were patients with very advanced stages of dementia, with presumably very low levels of awareness.

Also, some caution should be used when interpreting the findings of the multiple multivariate logistic regression analyses, as there may be a risk of an accumulation of the Type I error rate, considering the large number of tests in the analysis. However, most relationships we found and discuss in our study appear to be relatively strong ($P < .005$ or less) and correspond with clinical practice. This is to be tested in future studies.

We believe that, despite these limitations, relevant insights are generated by this study in the thus far unexplored area of YOD in nursing homes.

Conclusion and Implications

In conclusion, this study shows a high prevalence of NPSs in nursing home patients with YOD, correlated with dementia severity, dementia subtype, and disease awareness.

These variables are patient or disease characteristics that cannot be influenced. The high prevalence of NPSs results in the need to deliver care to patients with YOD in specialized care units, with skilled staff especially equipped to manage and reduce NPSs. NPSs should be paid appropriate attention to in diagnosis, treatment, support, and psycho-education of patients with YOD and caregivers. As in LOD, apathy and agitation are the most important symptoms to focus on. This is the first study to describe the prevalence and correlates of NPS in institutionalized patients with YOD. More research is needed to understand patient-related correlates (of which pain may be important⁴¹), and environmental correlates of NPS.

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